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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/443,986	11/19/1999	DANIEL JOSEPH OMAHONY	99.1064.US	8043

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Marilou E. Watson
Synnestvedt & Lechner LLP
2600 ARAMARK Tower
1101 Market Street
Philadelphia, PA 19107-2950

EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 05/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/443,986	OMAHONY, DANIEL JOSEPH	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *114,117-136 and 139-144* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *114,117-136 and 139-144* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 November 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 17, 2006 has been entered.

2. Applicant's response to the Office Action mailed January 18, 2006 on February 17, 2006, is acknowledged.

Claim Disposition

3. Claims 1-113, 115-116 and 137-138 have been cancelled. Claims 114, 117-136 and 139-144 are pending and are under examination.

Withdrawn-Specification Objections

4. Previous objection to the specification are withdrawn by virtue of submission of an amendment.

New-Specification Objection

5. The specification is objected to because of the following informalities:

The specification is objected to because on page 5, line 5 the following typographical error appears, "derivitives" which should be "derivatives". See also page 6, line 1 for "derivitization" which should be "derivation".

New-Claim Rejections - 35 USC 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

6. Claims 114, 117-125, 127-128 and 132-133 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 114 and the dependent claims hereto are drawn to a retro-inverted peptide, which reads on a product of nature. The claims do not clearly set forth that the peptides are synthesized as described in the instant specification on page 2. As natural mutations can occur and the claims do not clearly set forth that the peptides are not found in nature, the claims require clarification. The claims should be amended to indicate the hand of the inventor, for example the insertion of isolated or purified or synthetic in connection with the peptides to identify a product not found in nature (see MPEP 2105), (i.e. "A synthetic retro-inverted peptide").

Maintained-Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 114, 117-136 and 139-144 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 114 and the dependent claims hereto are directed to a retro-inverted peptide comprising SEQ ID NOS:1-3; said sequences are 15, 16 and 14 amino acids in length, respectively, wherein said peptide binds to a gastro-intestinal tract transport receptor (i.e. HPT1, hPEPT1, D2H, and hSI. The claims recite the open language of comprising which indicates that fragments can be added to the sequences in claim 114 on the N and C terminus as exhibited in claims 117-120. The claims encompass a genus of peptides. Note that claims 117-120 require expansion of the 15, 16 and 14 residues to 50, 40, 30 or 20 residues and claim 114 recites "comprising an amino acid

sequence selected from..." which is open and has no upper limit. Thus, the claimed genus is highly variable and not adequately described. The instant specification in tables 1-3 demonstrate the activity of peptides that are 15-mer, 14-mer and 16-mer. It is noted that two full-length sequences are compared (SEQ ID NO:7 and 8, i.e. 40-mer) to the retro-inverted peptide, however, the instant specification does not exemplify peptides that are 20-mer, or 50-mer (claim 117) or greater (claim 114) having activity. It is noted that the amended claims recite a structure and function, however, no correlation is made between structure and function of the fragments encompassed in the claims via demonstration of retention of function for all the fragments encompassed in the breath of the claims to demonstrate possession of the genus of the claimed invention. In addition, the specification lacks adequate description with respect to where in the structure of the receptors recited in the claims the peptide will bind. For example, hPEPT1 is known in the art to have 708 amino acids in the structure. Note that the WO98/51325 document relied upon disclose that the above receptor domains were cloned and expressed as His-tag fusion proteins, with the following amino acids in their domains "391-571 (hPEPT1); 29-273 (HPT1); 272-667 (hS1) and 387-685 (D2H). This appears to be the binding portion of the receptors, however, the instant specification lacks guidance with regard to this aspect of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. See *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997).*

In addition, claim 126 and its dependent claims are directed to a composition comprising a chimeric protein that comprises the retro-inverted peptide that is bound to an active agent, said active agent being of value in the treatment of a mammalian disease or disorder selected from the group consisting of hypertension, diabetes, osteoporosis, hemophilia, anemia, cancer, migraine and angina pectoris. Claim 126 and its dependents reads on fragments of the peptides being of "value" in the treatment of a mammalian disease. Said value is not adequately described. Thus, the claimed invention as a whole is directed to a genus of peptides, for which the specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is*

now claimed" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of encoded proteins, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993). See MPEP 2163.*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

8. Claims 114, 117-136 and 139-144 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the retro-inverted peptide consisting of the specific sequences (SEQ ID NOS: 1-3), does not reasonably provide enablement for fragments of the claimed peptides or a composition being of value in the treatment of all the mammalian disease or disorder encompassed in the claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a

disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to:

I. Quantity of Experimentation Necessary:

The claimed invention is directed to a retro-inverted peptide and fragments of the claimed peptide (see for example claims 114 and 117-120). Claim 114 for example, is directed to a peptide that comprises an amino acid selected from SEQ ID NOS:1-3, which reads on a full-length sequence, however can have fragments added to the N or C terminus, with no upper limits. In addition, claims 117-120 are directed to fragments of the claimed peptides. The art recognizes that the structure-function relationship of a peptide can be dramatically affected by structural changes. For example, claims such as 117-120 recite "wherein the peptide comprises no more than 50 amino acid residues; no more than 40 amino acid residues; no more than 30 amino acid residues and no more than 20 amino acid residues" and there is no indication that these fragments will retain the activity or have a different biological activity; no indication of conserved regions or whether the sequence consists of 50 contiguous residues for instance. The claimed peptide consists of SEQ ID NOS: 1-3; said sequences are 15, 16 and 14 amino acids in length, respectively and there is no indication in the claims or the instant specification where in the structure the additions contemplated in claims 117-120 will occur or if the structure can tolerate such modifications. Moreover, the claims are directed to a composition, comprising a chimeric protein bound to a material comprising an active agent, said chimeric protein comprising the peptide fused to a second protein, in which the active agent is of value in the treatment of a mammalian disease, several of

which are recited in the claims (see claim 126, for example). Thus, the claimed composition includes fragments of the claimed peptides. A skilled artisan would have to engage in undue experimentation to be able to construct the peptides as claimed and test same for biological activity. Furthermore, there is no indicia as to how to ascribe value to the active agent, which is simply defined as a drug or the laundry listing of agents provided in the claims. The instant specification provides literal support for the laundry lists of agents, however, no exemplification is provided to enable utilization of the entire listing in the claimed composition. Neither the claims nor the specification provides any showing of the claimed fragments in association with the claimed invention to enable one skilled in the art to be able to practice the full scope of the claimed invention, without undue experimentation.

II. Amount of direction or guidance presented:

The specification does not provide adequate guidance to be able to practice the claimed invention commensurate in scope with the claims. To examine every fragment to determine function/biological activity would require undue experimentation. In addition, there is no indicia as to the binding specificity to the receptors and if the peptide fragments will retain the binding activity. Furthermore, no guidance is provided as to the claimed diseases or disorders in association with the claimed peptide/fragments and what value is to be placed to obtain a peptide/peptide fragment that results in treatment of the recited diseases/disorders.

III. Presence or absence of working examples:

The working example provided discusses an animal study involving the bioavailability of insulin (see for example page 26, Table 5 of the specification), however, this example does not provide support for the unspecified amount of fragments encompassed by the claims or all the diseases claimed. Therefore, it is difficult to ascertain the nature of the claimed invention from this one record.

IV. Nature of the Invention:

The nature of the invention is a retro-inverted peptide or fragment that specifically binds to gastro-intestinal tract receptor. However, the specification does not provide sufficient guidance/direction to enable the full scope of the claimed invention as the claimed derivative/fragment is not described by size, length or function.

V. State of the prior art and Relative skill of those in the art:

It is disclosed in the specification on page 3 that the applicants have found retro-inverted forms of the GIT targeting agents specific receptor sites *in vivo* and/or promote uptake of active agents and/or enhance active agent delivery across the GIT into the systemic circulation. The claims are directed to fragments of the peptides and no characteristics or attributes of these have been described. As the prior art is silent on the claimed sequences a high level of skill was required at the time the application was filed.

VI. Predictability or unpredictability of the art:

Since very little is known in the prior art about the nature of the invention, renders the art unpredictable. The claimed invention is directed to fragments and it is highly unpredictable to target sequences when embedded in other sequences. Thus, the specification should then give more details as to how to make and use the invention in order to be enabling.

VII. Breadth of the claims:

The breadth of the claims are very broad and encompass a wide range of diseases and any fragment of the claimed sequences (SEQ ID NOS: 1-3). The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of fragments and a plurality of agents and diseases/disorders without any association to the claimed composition. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858*

F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 117-121, 126 and 129 is rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claims 117-120 lack clear antecedent basis because no support was found in the instant specification for the language "comprises no more than 50 amino acid residues", for example. It is noted that the claims filed on November 19, 1999 had this language, however, no support is found in the specification. Note that "comprises" is open, however, "no more than" is closed. Thus it is suggested that the claims recite "peptide is no more than 50 amino acid residues".

Claim 121 is confusing as it is unclear how "the active agent is of value in the treatment". Is said value a cure of the disease/disorder? See also claim 126.

Claim 129 lacks clear antecedent basis for "the composition of claim 121 which increases the transport of the active agent", claim 121 recites "said active agent being of value in the treatment of mammalian disease or disorder.

Withdrawn-Claim Rejections - 35 USC ∋ 112

10. Previous rejection to claim 135 under 35 U.S.C. 112, second paragraph is withdrawn by virtue of submission of an amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 114 and 118-120 are rejected under 35 U.S.C. 102(e) as being anticipated by Alvarez et al. (U.S. Patent No. 6,703,362, May 15, 1998).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Alvarez et al. teach a protein (SEQ ID NO:49) that specifically binds to the gastro intestinal tract receptor HPT1 (SEQ ID NO:178), see claim 1 of the patent. The instant claim 114 reads on any fragment of SEQ ID NOS:1-3, which includes a dipeptide. The Alvarez et al. patent disclose (SEQ ID NO:49) which has a residues (His-Arg) which can be found in the instant SEQ ID NO:2 (dipeptide). In addition, claims 118-120 reciting no more than 40 or 30 or 20 residues is anticipated as the patent discloses in claims 3-5, "not more than 40 or 30 or 20 amino acids in length. Therefore, the limitations of the claims are met by this reference.

Response to Arguments

12. Applicant's remarks made in the amendment filed on February 17, 2006 has been considered. Note that new objections have been made to the specification. In addition, the rejections under 35 U.S.C. 112, first paragraph written description and enablement have been amended and maintained for the reasons stated above and herein. Note also that a new ground of rejection has been instituted under 35 U.S. C. 112, second paragraph, 101 and 102 for the reasons stated above. The discussion of the two rejections will be combined as applicant has overlapping arguments.

On page 8 of the response, applicant state that independent claim 114 and 126 from which all other claims depend have been amended to be directed to peptides which bind to a gastro-intestinal tract transport receptor selected from the group consisting of HPT1, hPEPT1, D2H and hSI. It is further stated that as a consequence of

this amendment applicant submits that this functional language further defines the present invention. The instant invention is directed to a retro-inverted peptide comprising an amino acid sequence selected from SEQ ID NOS: 1-3 which are 15-mer, 16-mer and 14-mer. However, the claim reads on fragments of the claimed sequence and the claimed invention is directed to peptides that are no more than 50, 40, 30 or 20 residues. Claim 114 now recites that the peptide binds to a GIT receptor, for example hPEPT1 which is known in the art to have 708 amino acids in the structure. Note that the WO98/51325 document relied upon disclose that the above receptor domains were cloned and expressed as His-tag fusion proteins, with the following amino acids in their domains "391-571 (hPEPT1); 29-273 (HPT1); 272-667 (hS1) and 387-685 (D2H). This appears to be the binding portion of the receptors, however, the instant specification lacks guidance with regard to this aspect of the claimed invention. In addition, the claims comprise a genus of fragments not adequately described. Further, claims 121 and 126 are directed to compositions for treatment comprising an active agent being of value in a treatment of mammalian disease/disorder and the claims do not set forth what value to place on the active agent or demonstrate said composition in association with the laundry list of diseases/disorders.

Applicant's comments on page 9 are noted but are not persuasive. The instant claims are directed to a retro-inverted peptide comprising the above sequences (claim 114) wherein the peptide can comprise no more than 50 amino acids (claim 117); no more than 40 amino acids (claim 118), no more than 30 amino acids (claim 119); no more than 20 amino acids (claim 120); and a composition comprising the peptide bound

to material comprising an active agent being of value in the treatment of the recited diseases in claim 121 and the active agents are listed in claims such as 126. The claims recite the open language of comprising which indicates that fragments can be added to the sequences in claim 114 on the N and C terminus and claims such as claims 117-120 are directed to fragments of the claimed sequences and there is no recitation of function for the full-length sequences or the fragments. Note that there is no requirement for the 50 or 40 or 20 amino acids recited in the claims to be contiguous. There is no indication of a conserved region. Moreover, the peptide is in a composition comprising an active agent that is said to have value in treating diabetes, osteoporosis, angina pectoris, cancer, anemia, hemophilia, hypertension and migraine and the instant specification does not provide any showing of a drug with the claimed peptide in dosage form to treat any of the above diseases. Further, there's no showing that protein exists in altered forms in the diseases listed, for example, an over production or deficiency. In other words, the specification does not disclose that the peptide is expressed in cancer tissues for example, at altered levels or forms. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Absent a disclosure of altered levels or forms of a gene in diseased tissue as compared with the corresponding healthy tissue, the gene is not a disease marker or an appropriate target for drug discovery or toxicology testing. The specification provides a laundry list of active agents, however, there is no one to one correlation made between the claimed peptide and the diseases listed. Furthermore, the claims recite the language, "active agent being of value in the treatment" and there is no indication of what value the active agent

plays. Thus, in view of the foregoing the claimed invention requires undue experimentation, for a skilled artisan to practice the invention commensurate in scope with the claims and lacks adequate written description pertaining to the invention. Applicant has not demonstrated possession of the genus of peptides encompassed in the claims or demonstrated such in a medicament. Therefore, the rejections have been maintained.

Conclusion

13. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner 4/26/06

HOPE ROBINSON
PATENT EXAMINER